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EXAMINER	
BORIN, MICHAEL L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/730,214	MILLER ET AL.	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-26 and 28-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-26, 28-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Amendment filed 12/02/2003 is acknowledged. Claim 27 is canceled. Claims 22-26, 28-40 are pending. There are no amendments to the claims, except for claim dependency of claim 28.

2. As was stated in the previous Office action, in view of plurality of issues addressed in rejections under 35 U.S.C. 112,first and second paragraphs, it was deemed necessary to resolve these issues prior to applying appropriate art rejections. This does not mean as surmised by applicant that the pending claims are free of prior art.

Claim Rejections - 35 USC § 112, second paragraph.

3. Claims 22-26,28-40 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejections are maintained for the reasons of record which are reiterated below together with responses to arguments.

A. Claim 22, step three ("normalizing"), and claim 33: According to specification (p. 9), "normalizing" is dividing surface exposure of each amino acid by total surface exposure of the configuration. This is not clear because the preceding method step merely selected the peptide backbone based on set of angles. The backbone is a connection of -NH-(CH2)-CO- moieties, no amino acids are involved in the preceding step, so it is not clear how the surface "of each amino acid" can be estimated. Further, it is not clear what is a "total surface" as related to the backbone.

Response to arguments

Applicant argues that normalization step refers to backbone configurations that are comprised of amino acid sequences. Examiner maintains, however, that the common meaning of a backbone of a protein is a connection of -NH-(CH2)-CO- moieties without any specifics of side chains of amino acid residues; consequently , as no "real" no amino acids are involved in the method steps preceding to step three of claim 22, it is not clear how the surface "of each amino acid" can be estimated. Applicant's reference to p. 7 of specification is not convincing as it discusses Fig. 1, the latter depicting exactly what was meant by the rejection, i.e., connection of -NH-(CH2)-CO- moieties without any specifics of side chains of amino acid residues.

B. Claim 22, step four ("generating"): The term "random set of sequences" in regard to hydrophobicities, is indefinite because it is not clear what constitutes a "random set"; the term is not defined either in the art or in the specification (p. 9). It is not clear how the set is generated and applied.

Further, the term "uniform weight" is similarly indefinite. It is not clear how "uniform weight" is defined, how it affects generation of the set of sequences of hydrophobicities.

Further, the term "allowed sequences" is not clear. At which point the sequences are identified as "allowed", after the "normalizing" step, or they are sequences from the "random set of sequences of hydrophobicities"?

Response to arguments

First, applicant discusses hydrophobicities of amino acids. Again, as addressed in the rejection A) above, the claims do not address protein backbone, without any specifics of side chains of amino acid residues. Therefore, it is not clear what hydrophobicities are meant.

Further, the meaning of the term "sequence of hydrophobicities" is not clear: what is a "sequence" in relation to hydrophobicities, how it is generated (description that it is "randomly generated", as explained in the specification, p. 7 last paragraph, is not clear). Applicant argues that generation of a random set of values is a well

known technique. Applicant is invited to provide references supporting the fact that "random generation of sequences of hydrophobicities with uniform weight on the space of the allowed sequences" (as stated on p. 7 last paragraph) is indeed a well known technique fully appreciated by skilled artisan.

In regard to the use of the term "allowed sequences", applicant did not provide any explanations.

In regard to the term "uniform weight", applicant explains that it refers to "spacing between amino acids" and refers to p. 9, lines 23-32. Examiner failed to allocate there any such explanation of the term.

C. Claim 22, step six ("determining"): the step is vague and indefinite: first it recites one particular configuration ("ground state configuration"), then it addresses plurality of configurations ("desirable configurations"). Further, beginning of the description of the method step suggests that one configuration corresponds to one sequence, but following part of the phrase suggest that many sequences can fall within one configuration. Accordingly, beginning of the claims step addresses ground state of one configuration, while the end recites ground state of "configurations".

Response to arguments

Applicant states that the step determines which configuration comprises a ground state. It is not clear how a configuration may "comprise" a ground state. It remains unclear how beginning of the claims step addresses ground state of one configuration, while the end recites ground state of "configurations".

D. Claim 22, step seven ("synthesizing"). First, it is not clear what "amino acids" are being addressed: the preceding parts of the claim discuss only a backbone (i.e., a string of -NH-(CH2)-CO- moieties) and do not address any amino acids. Second, for which of the plurality of different "configurations" addressed in the claim, the sequence is synthesized. Finally, as all configurations addressed in the claim differ in their spatial configuration, not their structure, how the preceding steps of the claim relate to the step of "synthesizing"?

Response to arguments

Applicant informs that any art recognized method of protein synthesis may be employed. The question, however, is not how to synthesize a protein, but what it is to be synthesized as the claim discuss only a backbone (i.e., a string of -NH-(CH2)-CO- moieties) and do not address any amino acids. Further, applicant does not answer the questions for which of the plurality of different "configurations" addressed in the claim, the sequence is synthesized. Finally, as all configurations addressed in the claim

differ in their spatial configuration, not their structure, how the preceding steps of the claim relate to the step of "synthesizing"?

F. Claims 28,35: it is not clear what is "non-compact" configurations, which configurations fall within the scope of the term, and how such configurations are eliminated.

Response to arguments

Applicant directs attention to p. 8, last paragraph. However, this paragraph addresses determination of compactness for amino acids, whereas the claims, as discussed above address computations of backbone configurations. Further, the cited reference of Flower et al address calculation of total surface area, not compactness.

G. Claims 29,36,38: the term "sufficiently similar" is indefinite because it is a relative term, but no standard of reference has been provided with which to determine whether a particular configuration is sufficiently similar or not. Accordingly, it is not possible to determine what configurations are embraced within the scope of the claims.

Further, it is not clear from the claim how "clustering configurations" is "followed by their backbones".

Further, it is not clear from the claim which "treating" assumes that all configurations in a cluster as a single configuration.

Further, the term "designability of the cluster" and its involvement in the method step, is not clear.

Response to arguments

Applicant directs attention to p.10, line 19 through p. 11, line 5. This text, however, does not present clear answers to the questions above.

H. Claims 30,34: which "each configuration" is addressed? Further, how can "designing proteins" start from configurations identified in claims 30,34 if the preceding claims identified a number of steps which has to be executed first before arriving to the step of claims 30,34.

Response to arguments

Applicant responds that "each configuration" refers to clustered configuration of the preceding claim. First, claim 34 depends on claim 22 which does not recite any "clustered configuration". As to claim 30, it does not specify that "each configuration" means each of the clustered configurations; contrary, the preceding

claims recite plurality of various configurations, and it is not clear which one is addressed in claim 30.

As for the issue of from which step "designing of proteins" begins, applicant responds that it refers to selection of proteins having the highest variance. Examiner maintains, however, that the preceding claims identified a number of steps of protein design that has to be executed first before arriving to the step of claims 30,34, it is not clear how the design "begins" only after the step of claims 30 or 34 has been executed.

Claim Rejections - 35 USC § 112, first paragraph.

4. Claims 22-26,28-40 remain rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The rejection is maintained for the reasons of record.

Examiner maintains that selection of amino acid components of the protein to be designed is critical or essential to the practice of the invention, but not included in the claims and is not enabled by the disclosure. The only criteria as claimed for generating backbone configuration is selection of dihedral angle pairs. Based only on combination of angles, and backbone configuration without any information on particular amino acid residues and their side chains, an artisan will not be capable of

implementing subsequent method steps, such as determining hydrophobicities, evaluating energy, and synthesizing (undefined) protein sequences.

Claim Rejections - 35 U.S.C. § 101/ 112-1

5. Claims 22-26,28-40 remain rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a substantial utility or a well established utility. The rejection is maintained for the reasons of record (see previous Office action).

Applicant submits that "the pending claims serve to clarify the utility of the claimed invention". As there are no amendments to the claims, there is no further "clarification", and the claims remain rejected for the reasons of record.

6. Claims 22-26,28-40 also remain rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

Conclusion.

7. No claims are allowed

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0549.

March 8, 2004

mlb

MICHAEL BORIN, PH.D
PRIMARY EXAMINER